

Individual variation in body temperature and energy expenditure in response to mild cold

Citation for published version (APA):

van Marken Lichtenbelt, W. D., Schrauwen, P., van de Kerckhove, S., & Westerterp-Plantenga, M. S. (2002). Individual variation in body temperature and energy expenditure in response to mild cold. *American Journal of Physiology : Endocrinology and Metabolism*, 282(5), E1077-E1083. <https://doi.org/10.1152/ajpendo.00020.2001>

Document status and date:

Published: 01/01/2002

DOI:

[10.1152/ajpendo.00020.2001](https://doi.org/10.1152/ajpendo.00020.2001)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Individual variation in body temperature and energy expenditure in response to mild cold

WOUTER D. VAN MARKEN LICHTENBELT, PATRICK SCHRAUWEN,
STEPHANIE VAN DE KERCKHOVE, AND MARGRIET S. WESTERTERP-PLANTENGA
Department of Human Biology, Maastricht University, 6200 MD Maastricht, The Netherlands

Received 22 January 2001; accepted in final form 2 January 2002

Marken Lichtenbelt, Wouter D. van, Patrick Schrauwen, Stephanie van de Kerckhove, and Margriet S. Westerterp-Plantenga. Individual variation in body temperature and energy expenditure in response to mild cold. *Am J Physiol Endocrinol Metab* 282: E1077–E1083, 2002. First published January 8, 2002; 10.1152/ajpendo.00020.2001.—We studied interindividual variation in body temperature and energy expenditure, the relation between these two, and the effect of mild decrease in environmental temperature (16 vs. 22°C) on both body temperature and energy expenditure. Nine males stayed three times for 60 h (2000–0800) in a respiration chamber, once at 22°C and twice at 16°C, in random order. Twenty-four-hour energy expenditure, thermic effect of food, sleeping metabolic rate, activity-induced energy expenditure, and rectal and skin temperatures were measured. A rank correlation test with data of 6 test days showed significant interindividual variation in both rectal and skin temperatures and energy expenditures adjusted for body composition. Short-term exposure of the subjects to 16°C caused a significant decrease in body temperature (both skin and core), an increase in temperature gradients, and an increase in energy expenditure. The change in body temperature gradients was negatively related to changes in energy expenditure. This shows that interindividual differences exist with respect to the relative contribution of metabolic and insulative adaptations to cold.

temperature gradient; thermoregulation; respiration chamber; metabolic adaptation; insulative adaptation

STUDIES ON THE EFFECT OF AMBIENT TEMPERATURE on metabolism in humans often concentrate on either energy expenditure (7) or body temperature (14). Although there are many studies that examine cold exposure in rodents and humans, relatively few studies have looked at the interaction of energy metabolism and body temperature under more moderate conditions, such as met in daily life (13, 17, 18). It is generally acknowledged that a low resting metabolic rate is a risk factor for weight gain (16). In this respect, much less attention is given to relatively low body temperatures, although animal studies indicate that low body temperature may be a risk factor for obesity (5), and, second, there are indications for associations between body temperature and metabolic rate in humans (13, 18).

When we study body temperature, it is important to recognize that different sites of the body have different temperatures and that their responses to a variation in environmental temperature are site specific. The body can be divided roughly into two compartments: the thermal core and the thermal shell (2). Most of the energy produced within the core is dissipated into the environment via the body surface. It follows that, under thermoneutral conditions (16 to 28°C, with the human body dressed), the skin temperature is lower than the core temperature and the skin temperature varies more with the ambient temperature.

Theoretically, three types of thermoregulatory adjustments have been described during long-term adaptation to a colder environment (11): hypothermic adaptation (lowered thermoregulatory set point), insulative adaptation (subcutaneous fat and/or more efficient vasoconstriction), and metabolic adaptation (or nonshivering thermogenesis).

Individuals may differ in their physiological adaptations to environmental changes. For instance, during short-term exposure to mild cold, people may differ in their response to the relative contribution of these adaptations, especially the insulative and metabolic ones.

Indeed, exposure to mild cold has been shown to increase the temperature gradient, i.e., a reduction of peripheral temperature at relatively constant core temperature (8), whereas other studies showed that energy metabolism increased (3, 7). However, the combination, i.e., measuring the components of energy expenditure together with body temperature distribution in response to mild cold, has not before been studied in detail.

In the present study, we aim to examine the interindividual set points in body temperature and energy expenditure to determine whether individual variation in energy expenditure is related to body temperature and to investigate the effect of a mild decrease in environmental temperature (16 vs. 22°C) on both body temperature and energy expenditure.

Address for reprint requests and other correspondence: W. D. van Marken Lichtenbelt, P. Schrauwen, and/or M. S. Westerterp-Plantenga, Dept. of Human Biology, Maastricht Univ., PO Box 616, 6200 MD Maastricht, The Netherlands (E-mail: MarkenLichtenbelt@HB.unimaas.NL; P.Schrauwen@HB.unimaas.NL; M.Westerterp@HB.unimaas.NL).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

MATERIALS AND METHODS

Nine healthy male Caucasian volunteers participated in the study. They had grown up and were now living in the Netherlands. Body mass was 76.2 ± 9.4 kg, body mass index amounted to 22.7 ± 2.1 kg/m², percent body fat was $17.9 \pm 5.4\%$, and age was 23.8 ± 5.1 yr. The Medical Ethics Committee of Maastricht University approved the study.

Body composition. Whole body density was determined by underwater weighing in the morning of subjects in fasted state. Body weight was measured with a digital balance with an accuracy of ± 0.01 kg (Sauter, type E1200). Lung volume was measured simultaneously with the helium dilution technique by use of a spirometer (Volugraph 2000, Mijndhardt). Percent body fat was calculated using the equation of Siri (23). Fat-free mass in kilograms was calculated by subtracting fat mass from body mass.

Energy expenditure. Each of three tests lasted for 60 h. The test took place in a 14-m³ respiration chamber, as described in detail by Schoffelen et al. (19). The room was ventilated with fresh air. The ventilation rate was measured with a dry gas meter (G4 Schlumberger, The Netherlands) and amounted to 70–80 l/min. The relative humidity was set at 55% at both 22 and 16°C. Physical activity was monitored by means of a radar system based on the Doppler principle; the sensitivity of this radar system is described by Schoffelen et al. (19). Twenty-four-hour energy expenditure (24-h EE) was determined from the subject's O₂ consumption and CO₂ production, according to the formula by Weir (25). Five-minute measurements were used to calculate mean 30-min values (4, 19). Sleeping metabolic rate (SMR) was calculated as the lowest mean energy expenditure over three consecutive hours between 2400 and 0700. Twenty-four-hour thermic effect of food (TEF) was determined as the increase in EE above SMR, corrected for activity-induced EE (AEE). This was achieved by plotting EE against radar output. The intercept of the regression line at the offset of the radar, thus at zero physical activity, represents the EE in the inactive state: resting energy expenditure (RMR), which is equal to SMR plus TEF. TEF was calculated by subtracting SMR from RMR (26). AEE was obtained by subtracting TEF and SMR from 24-h EE. The physical activity index (PAI) was calculated as 24-h EE/SMR.

Body temperature. Subjects' skin temperatures were measured continuously from 0800 until 2400 by means of thermistor surface contact probes [series 400, type 409B, Yellow Springs Instrument (YSI); accuracy $\pm 0.1^\circ\text{C}$] fixed on the skin with thin, air-permeable, adhesive surgical tape. The probes were applied to the following standardized regions: forehead, ventral side of the liver, and nondominant sides of thigh, hand, and foot. Distal skin temperatures were calculated from means of temperatures of hand and foot, and proximal skin temperatures were derived by averaging temperatures of forehead, liver, and thigh. The thermometric probes were calibrated to within 0.05°C in a water bath against a reference mercury thermometer (accuracy: $\pm 0.02^\circ\text{C}$).

For the core temperature, the subjects measured their rectal temperature each 30 min by means of a conventional digital thermometer (Philips HP 5315, accuracy $\pm 0.1^\circ\text{C}$) that was inserted 3.5–4 cm from the anal sphincter. From 2400 until 0800, rectal temperature was measured using thermistor probes (YSI series 400; accuracy $\pm 0.1^\circ\text{C}$). (At 22°C, the night rectal temperature measurement of one subject is missing.) Measurements were done every 4 min, and from these, 30-min values were calculated. Temperature measurements were thoroughly explained to the subjects before they entered the respiration chambers. Simultaneous measure-

ments (i.e., within 5 min) with both thermometers were carried out in the mornings and evenings. These measurements revealed good agreement ($r = 0.86$, $P < 0.0001$) under the experimental conditions of this study, with a mean difference (bias) of 0.09°C (Phillips minus YSI) and a standard deviation (or error) of 0.2°C ($n = 39$).

Temperature gradients were calculated as the differences between core temperature and proximal skin temperature, core temperature and distal skin temperature, and proximal and distal skin temperatures.

Protocol. The study took place at the Department of Human Biology, Maastricht University, during the winter season from November 1998 to March 1999. Subjects stayed three times for 60 h each (2200–0800) in the respiration chamber, once at 22°C and twice at 16°C, in random order (Fig. 1). The first night was for acclimation, and the data analyses were carried out twice for 24 h from 0800 to 0800. Body weight was determined before and after each stay in the chamber, and the subjects weighed themselves each morning in fasted state after voiding. The interval between each stay in the chamber was from 1 to 4 wk.

At 22°C and once at 16°C, subjects were fed in energy balance (EB) on the 1st day and ad libitum (AL) on the 2nd day (22EB, 22AL; 16EB3, 16AL; Fig. 1). The other time at 16°C, subjects were fed in EB during both days (16EB1, 16EB2). This experimental setup allowed us to correct for the possible acclimation effects of a lowered ambient temperature on EE. For pairwise comparison of 22 and 16°C, 16EB2 (day 2) was compared with 22EB, and 16AL with 22AL.

Feeding in energy balance was based on individually calculated energy requirements: after measurement of SMR during the first night in the respiration chamber, an estimated 24-h energy requirement was calculated by multiplying SMR with a PAI of 1.65 (21). Twenty-four-hour energy intake was 12.7 ± 2.0 MJ at 16°C and 11.9 ± 2.2 MJ at 22°C. Food composition and regimens at 22 and 16°C were identical. Macronutrient composition, by percent energy for carbohydrate, protein, and fat, was 49:15:36.

The clothing was identical during all experiments and was tested before each protocol began to assure comfort at 16°C as well as at 22°C. During the day (0800–2400), the outfit consisted of 1 T-shirt, 1 cotton shirt, 1 jogging shirt (70% cotton, 30% polyester), 1 pair of jogging trousers (50% cotton, 50% polyester), and a pair of sport shoes. Subjects did not wear socks. The total insulative capacity of the clothing amounted to 0.71 Clo. At night (2400–0800), subjects were

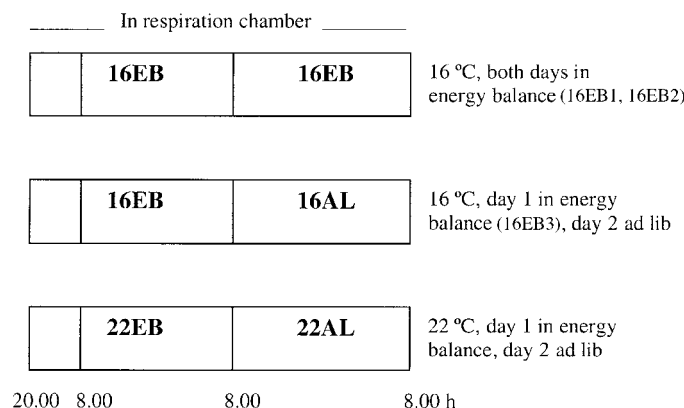


Fig. 1. The study design. Subjects stayed 3 times for 60 h each time in the respiration chamber. Twenty-four-hour data were analyzed from 0800 to 0800.

Table 1. *Body temperatures of rectum and skin (distal and proximal) and body temperature gradients*

	16°C EB1 day 1	16°C EB2 day 2	16°C EB3 day 1	16°C AL day 2	22°C EB day 1	22°C AL day 2	<i>P</i> values by ANOVA		
							Subjects	Temp	Diet
T _{rec} 24h	36.7 ± 0.4	36.7 ± 0.4 ¹²	36.7 ± 0.3 ³⁴	36.7 ± 0.4	36.8 ± 0.3 ¹³	36.9 ± 0.2 ²⁴	0.0001	0.001	NS
T _{rec} day	36.9 ± 0.5	36.9 ± 0.5	36.8 ± 0.5 ¹²	36.9 ± 0.6	37.1 ± 0.3 ¹	37.1 ± 0.3 ²	0.0001	0.0005	NS
T _{rec} night	36.5 ± 0.8	36.4 ± 0.2	36.3 ± 0.3	36.3 ± 0.4	36.5 ± 0.3	36.4 ± 0.3	0.01	NS	NS
T _{prox}	32.1 ± 0.8 ¹²	32.1 ± 0.9 ³⁴	31.9 ± 0.8 ⁵⁶	31.9 ± 1.0 ⁷⁸	33.3 ± 1.0 ¹³⁵⁶	33.4 ± 0.6 ²⁴⁶⁸	0.01	0.0001	NS
T _{dis}	27.8 ± 2.0 ¹²	27.7 ± 1.9 ³⁴	27.6 ± 1.4 ⁵⁶	27.9 ± 1.6 ⁷⁸	32.5 ± 0.8 ¹³⁵⁶	31.7 ± 1.7 ²⁴⁶⁸	0.002	0.0001	NS
T _{rec-dis}	9.1 ± 2.1 ¹²	9.2 ± 1.9 ³⁴	9.2 ± 1.7 ⁵⁶	9.0 ± 2.0 ⁷⁸	4.6 ± 0.7 ¹³⁵⁷	5.4 ± 1.7 ²⁴⁶⁸	0.0004	0.0001	NS
T _{rec-prox}	4.9 ± 1.0 ¹²	4.8 ± 1.0 ³⁴	5.0 ± 0.8 ⁵⁶	5.0 ± 1.2 ⁷⁸	3.7 ± 0.6 ¹³⁵⁷	3.6 ± 0.5 ²⁴⁶⁸	0.0014	0.0001	NS
T _{prox-dis}	4.3 ± 1.8 ¹²	4.5 ± 1.6 ³⁴	4.7 ± 1.6 ⁵⁶	4.1 ± 1.7 ⁷⁸	0.8 ± 0.6 ¹³⁵⁷	1.7 ± 1.6 ²⁴⁶⁸	0.0001	0.0001	NS

Values are means ± SD expressed in °C. T_{rec}, rectal temperature; T_{prox}, proximal temperature; T_{dis}, distal temperature; T_{rec-dis}, temperature gradient from T_{rec} and T_{dis}; EB, energy balance; AL, ad libitum; NS, not significant. Significant paired differences by paired *t*-test are shown by different superscript nos.

asked to wear a T-shirt and boxer shorts and to lie under a cotton sheet and duvet (375 g/m²). Daily activities were standardized by describing every hour, and sometimes every 15 min, what the subjects were supposed to do. These activities included household activities, extensive standardized aerobic exercise, and sedentary activities, such as reading and watching television. Also, meal and snack times were standardized.

Statistics. Body temperatures, temperature gradients, and EE components of the six test days (16EB1, 16EB2, 16EB3, 16AL, 22EB, 22AL) were compared using subjects, environmental temperature, and feeding regimen as independent variables with factorial analyses of variance (ANOVA). For post hoc pairwise comparisons, Student's *t*-test was used.

To assess the relationship between body temperature and energy metabolism, EE parameters were adjusted for body composition by performing multiple regression of energy expenditure (in MJ/day) against fat mass and fat-free mass (in kg) (15). For each subject, the adjusted metabolic rate (i.e., the residual) was calculated by subtracting the predicted value, by use of the regression equation, from the actually measured metabolic rate.

For tracking of the body temperatures or EE throughout the different experiments, individuals were ranked per test day. By ANOVA, it was investigated whether the ranking was consistent throughout the different days.

Statistical analyses were performed using STATVIEW SE+Graphics, ABACUS concepts (Berkeley, CA). Outcomes were regarded as statistically significantly different if *P* < 0.05.

RESULTS

Body temperature: individual differences. Variations in body temperature (rectal, proximal skin, and distal skin) were explained by individual differences and by environmental temperature (factorial ANOVA, Table 1). There was no significant effect of the feeding regimen on body temperatures. The site-specific skin temperature measurements revealed comparable results (data not shown).

Rectal temperatures on *day 1* and *day 2* during all experiments were significantly correlated, emphasizing individual specific body temperatures. This holds for 24-h rectal temperature (e.g., 16°C EB, *day 1* and *day 2*: $R^2 = 0.98$, $P < 0.0001$), as well as daytime rectal temperature (e.g., 16°C EB, *day 1* and *day 2*: $R^2 = 0.95$, $P < 0.0001$; see Fig. 2). For tracking the body temperatures throughout the different experiments, each in-

dividual was ranked according to body temperature. By ANOVA, this ranking was consistent throughout the different environmental temperatures or feeding regimens [24-h T_{rectal} (T_{rec}): $F = 37.6$, $df = 8$, $P < 0.0001$].

Ranking according to distal and proximal skin temperatures were also significantly consistent throughout the experiments [distal (T_{dis}): $F = 5.7$, $df = 8$, $P < 0.0001$; proximal (T_{prox}): $F = 8.9$, $df = 8$, $P < 0.0001$].

Body temperature: response to mild cold. At 16°C, mean proximal skin temperatures were 1.2–1.5°C lower than those at 22°C (Table 1). Body core temperature at 16°C was significantly $0.2 \pm 0.15^\circ\text{C}$ lower than at 22°C during EB only ($P < 0.02$).

Temperature gradients increased significantly at 16°C compared with 22°C (all *P* values < 0.005, Table 1).

Temperature gradients between days were also significantly related at 16°C (16EB1 and 16EB2, T_{rec}-T_{dis}: $R^2 = 0.80$, $P < 0.001$; T_{rec}-T_{prox}: $R^2 = 0.94$, $P < 0.0001$; for example, see Fig. 3). At 22°C only, T_{rec}-T_{prox} was related between *day 1* and *day 2* ($R^2 = 0.73$, $P < 0.01$).

The 22 to 16°C changes in body temperatures during EB were significantly related to those from AL experiments for daytime T_{rec} ($R^2 = 0.83$, $P < .001$). This indicates that not only body temperatures and body temperature gradients, but also the response to the

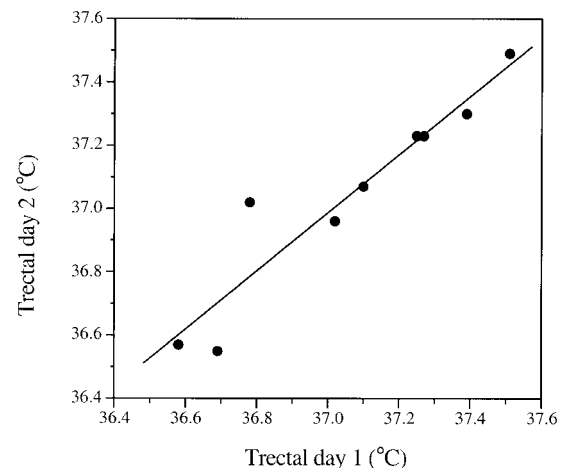


Fig. 2. Relationship between day-time rectal temperatures (T_{rectal}) on the two consecutive days at 22°C ($R^2 = 0.90$, $P < 0.0001$).

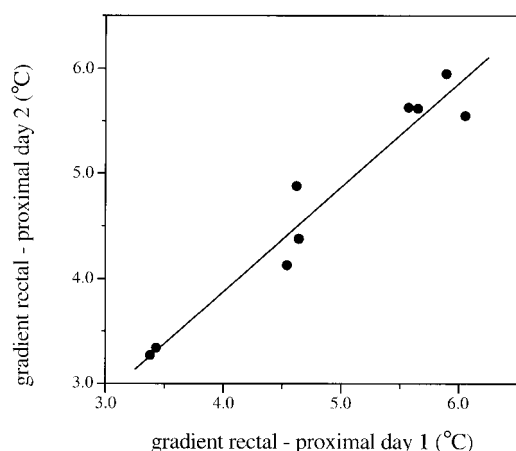


Fig. 3. Relationship between the gradients ($T_{\text{rectal}} - T_{\text{proximal}}$) on 2 consecutive days at 16°C during energy balance (EB, $R^2 = 0.94$, $P < 0.0001$).

changes in environmental temperature, showed inter-individual differences.

EE. EB (24-h energy intake minus EE) was not significantly different from zero during the EB test days but was significantly increased during AL feeding at both 16°C (4.54 ± 2.23 MJ/day, $P < 0.001$) and 22°C (4.07 ± 1.97 MJ/day, $P < 0.001$, Table 2).

Apart from individual differences in 24-h EE, there was a significant effect of environmental temperature and also an effect of the feeding regimen (factorial ANOVA $P < 0.05$, Table 2). The same accounts for the TEF and AEE. There were no significant effects of the environmental temperature and feeding regimens on SMR and the PAI. At 16°C, 24-h EE is increased compared with that at 22°C. This holds for the EB situation (16EB2 vs. 22EB) as for the AL (16AL vs. 22AL) situation. The increased TEF at 16°C compared with 22°C is significant only in the EB situation.

Twenty-four-hour EE and TEF were elevated during AL feeding compared with EB at both environmental temperatures (Table 2, compare 16EB3 and 16AL, and 22EB and 22AL).

Adjusted values of 24-h EE and SMR were significantly related between *day 1* and *day 2* within each test (Fig. 4, A and B). Comparing the results of the six test days also revealed that the adjusted 24-h EE and SMR values were significantly related (rank test 24-h

EE: $F = 35.70$, $df = 8$, $P < 0.0001$; SMR: $F = 41.11$, $df = 8$, $P < 0.0001$), which emphasized that EE is an individual trait, even after adjustment for fat-free mass and fat mass.

The 16–22°C changes in 24-h EE and SMR, adjusted for body composition from EB, were significantly related to those from AL experiments ($P < 0.01$ and $P < 0.05$, respectively).

Relations between body temperature and EE. At 22°C, 24-h EE and SMR, adjusted for body composition, were related to rectal temperature at *day 1* (24-h EE: $R^2: 0.46$, $P = 0.06$; SMR: $R^2: 0.54$, $P < 0.05$) and *day 2* (24-h EE: $R^2: 0.83$, $P < 0.005$, Fig. 5; SMR: $R^2: 0.64$, $P < 0.02$). AEE was related to rectal temperature on *day 2* only [AEE *day 1*: not significant (NS), AEE *day 2*: $R^2: 0.82$, $P < 0.005$]. SMR was related to rectal temperature at night on *day 1* only ($R^2: 0.62$, $P < 0.02$).

In search for acclimation effects, 16°C EB values on *day 1* and *day 2* were compared. Twenty-four-hour EE, TEF, and AEE were elevated on *day 2*. No apparent significant differences in body temperatures were found. However, clearly individual differences were evident: some individuals increased their gradient ($T_{\text{rec}} - T_{\text{prox}}$), whereas others decreased that gradient. Twenty-four-hour EE increased on average, but with large individual differences (mean change in 24-h EE: 0.8 ± 0.7 MJ/day). The relation between the change in temperature gradients was significantly negatively related to the change in 24-h EE (Fig. 6). This means that those subjects without or with little increase in 24-h EE showed no change or an increase in their body temperature gradient, whereas those that increased their 24-h EE showed a decrease in their body temperature gradient.

DISCUSSION

Short-term exposure of normal-weight men who were used to an ambient temperature of 22°C (normal temperature in the building and in most rooms in the Netherlands) to 16°C caused a significant decrease in body temperature (both skin and core), an increase in temperature gradients, and an increase in EE. It was demonstrated that both body temperatures and EEs adjusted for body composition were subject specific. This was shown by significant correlations between these measurements on the different test days and by

Table 2. Different components of energy expenditure and energy balance

	16°C EB1 day 1	16°C EB2 day 2	16°C EB3 day 1	16°C AL day 2	22°C EB day 1	22°C AL day 2	P Value by ANOVA		
							P	Temp	Diet
24-h EE	12.05 ± 1.60^{12}	12.91 ± 2.01^{234}	12.77 ± 1.90^5	13.38 ± 2.06^{13567}	12.17 ± 2.23^{468}	12.90 ± 1.97^{78}	0.0001	0.002	0.0001
SMR	7.53 ± 0.97	7.67 ± 1.08	7.59 ± 1.48	7.74 ± 1.07	7.44 ± 1.06	7.67 ± 0.92	0.0001	NS	NS
PAI	1.64 ± 0.11	1.68 ± 0.11	1.70 ± 0.10	1.73 ± 0.08	1.63 ± 0.13	1.68 ± 0.08	0.01	NS	NS
AEE	4.95 ± 0.83^{12}	5.32 ± 0.67^{23}	5.64 ± 0.98	6.91 ± 3.58^1	4.43 ± 1.35^{134}	5.37 ± 1.18^4	0.0001	0.02	0.0041
DIT	1.34 ± 0.51^1	1.71 ± 0.41^{23}	1.25 ± 0.51^{24}	1.62 ± 0.49^{25}	0.95 ± 0.51^{1356}	1.63 ± 0.61^6	0.0009	0.04	0.002
EB	0.89 ± 0.96^{1234}	-0.22 ± 0.99^{156}	-0.021 ± 0.96^{278}	$4.54 \pm 2.23^{3579*}$	-0.25 ± 0.85^{90}	$4.07 \pm 1.97^{4680*}$	0.0002	NS	0.0001

Values are means \pm SD expressed in MJ/day. EE, energy expenditure; SMR, sleeping metabolic rate; PAI, physical activity index; AEE, activity-induced energy expenditure; DIT, diet-induced EE. Significant paired differences by paired *t*-test are shown by different superscript nos. from 0 to 9; *, a single digit beyond 9.

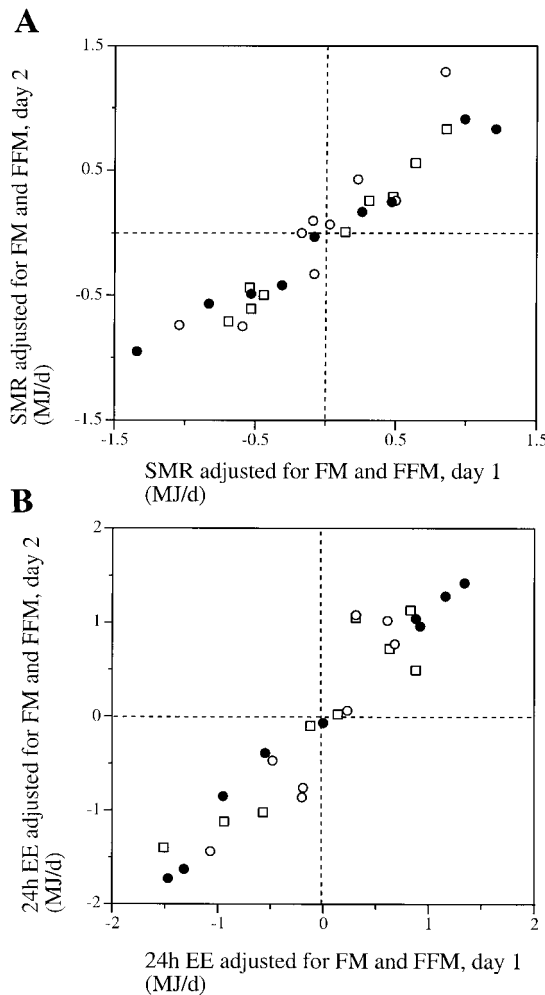


Fig. 4. A: relationships between sleeping metabolic rates (SMR), adjusted for fat mass (FM) and fat-free mass (FFM), on 2 consecutive days. Adjusted SMR is depicted as the residual from the relationship of SMR against FM and FFM. Data from all experiments: \bullet , 16°C, EB, $R^2 = 0.97$, $P < 0.0001$; \circ , 16°C, EB-AL, $R^2 = 0.85$, $P < 0.0005$; \square , 22°C, $R^2 = 0.98$, $P < 0.0001$. B: relationships between 24-h EE, adjusted for FM and FFM, on 2 consecutive days. Adjusted 24-h EE is depicted as the residual from the relationship of SMR against FM and FFM. Data from all experiments: \bullet , 16°C, EB, $R^2 = 0.99$, $P < 0.0001$; \circ , 16°C, EB-AL, $R^2 = 0.82$, $P < 0.005$; \square , 22°C, $R^2 = 0.86$, $P < 0.0005$.

a rank correlation test comparing the results from six different test days. EEs (24-h EE and SMR adjusted for body composition) were significantly related to body core temperature (T_{rec} 24-h and T_{rec} night, respectively). In response to mild cold, the change in body temperature gradients was negatively related to changes in EE. This shows that interindividual differences exist with respect to the relative contribution of metabolic and insulative adaptations to cold.

Individual differences in body temperature. Studies on interindividual variation in body set point temperature in humans are very scarce. One of the oldest studies on a large group is from Wunderlich (27). Although this study noted individual differences in axillary body temperature, it was not until 1992, when Rising et al. (18) in their reexamination of the Minne-

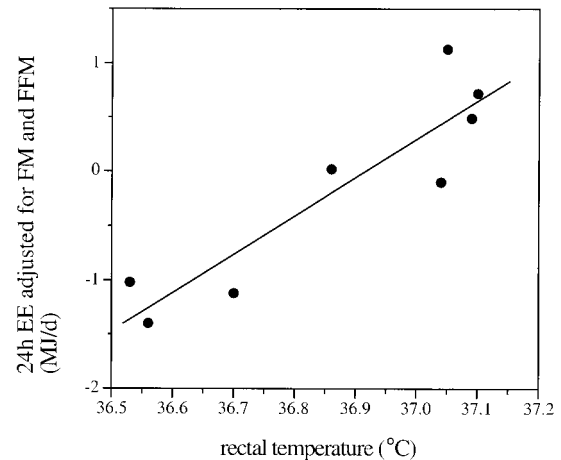


Fig. 5. Twenty-four-hour (24-h) EE, adjusted for FM and FFM, plotted against rectal temperature ($R^2 = 0.83$, $P < 0.002$). Adjusted 24-h EE is depicted as the residual from the relationship of SMR against FM and FFM.

sota semi-starvation study showed that (oral) body temperatures varied more between individuals than can be attributed to intraindividual variance. Recently we showed interindividual variation in tympanic temperature in a study in women in which the environmental temperatures of 27 and 22°C were compared (13). Oral and tympanic (by infrared sensor) temperatures may not be representative measures of core temperature. In situations in which body temperatures do not fluctuate very fast, core temperature can be measured rectally (24). Our data on significant interindividual variance in rectal temperature thus provide the strongest evidence so far that, indeed, different individuals regulate body temperature to different set points.

Individual differences in EE and relation to body temperature. The largest ranges in adjusted 24-h EE and SMR were -1.73 to 1.42 MJ/day (during 16°C AL) and -1.34 to 1.21 MJ/day (during 16°C EB), respec-

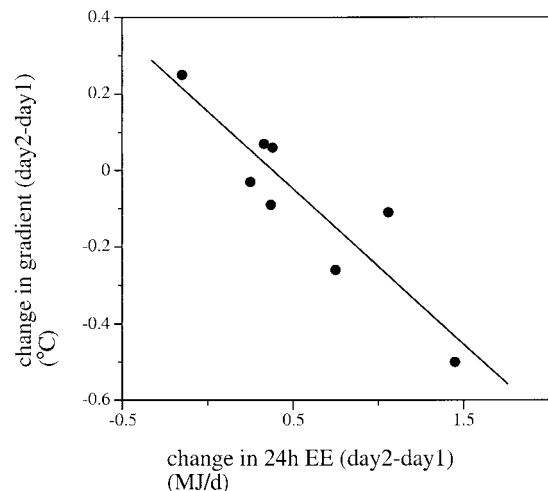


Fig. 6. Changes from day 1 to day 2 in body temperature gradient ($T_{\text{rectal}} - T_{\text{proximal}}$) plotted against changes in 24-h EE ($R^2 = 0.82$, $P < 0.002$). Data from EE experiment at 16°C (16EB1 and 16EB2).

tively. The range of SMR (2.6 MJ/day), which might be diminished because of cover use during the night, approaches the range reported for Pima Indians of 3 MJ/day (18). Regression analyses and rank correlation both showed significant interindividual variance in adjusted 24-h EE, SMR, and AEE. Thus, as with body temperature, the relative level of EE is individually specific, possibly genetically determined. We have shown previously that uncoupling proteins might be one of the determinants underlying the variation in SMR adjusted for fat-free mass (22). The magnitude of the range in EE just mentioned has large physiological and clinical consequences, as shown by Rising et al. (18) and Ravussin et al. (16).

In search for relations between body temperature and EE, we used the data of the 22°C test, which could be considered to be the subjects' habitual environmental temperature. Indeed, 24-h EE and SMR, adjusted for body composition, were related to 24-h rectal temperatures. Adjusted SMR values were related to night rectal temperatures on *day 1*. It follows that the relation between 24-h EE and rectal temperature can partly be explained by the relation between SMR and night temperatures. Apart from SMR, the relation between 24-h EE and body temperature can be explained by activity. Indeed, adjusted AEE was significantly related to 24-h T_{rec} on *day 1*. As indicated previously (13), because the daily activities protocol was standardized, the differences in AEE can be explained by the so-called nonexercise activity thermogenesis, or NEAT (12). The relative contribution of AEE and RMR to the relation between 24-h EE and body temperature is difficult to unravel. Stepwise regression indicates a significant contribution of SMR to 24-h T_{rec} , without inclusion of AEE. Of course, body temperature is an effect not only of EE, but also of (individual differences in) heat dissipation, which is subject to further investigation.

Response to mild cold. The slight but significant decrease in core body temperature at 16°C relative to 22°C, combined with much larger decreases in skin temperatures, conforms to earlier studies: mild cold was shown to increase the temperature gradient, i.e., a reduction of peripheral temperature at relatively constant core temperature (8). Our results indicate that the increase in 24-h EE can be attributed to the increases of TEF, AEE, and possibly nonshivering thermogenesis.

Adjacent to our finding that different individuals regulate body temperature to different set points, our data indicate that changes in body temperature in different situations are individual specific. This is shown by the significant relation between changes in skin temperature from 22 to 16°C in the comparison of *days 1* and *2*. Although differences in response to (mild or more severe) cold between groups have been reported before (1, 9, 10, 20), to our knowledge this relation has not been shown before on an individual level within a population.

In response to the mild cold, 24-h EE increased slightly (EB: $\Delta\text{EE} = 0.74$ MJ/day; AL: $\Delta\text{EE} = 0.48$

MJ/day) but significantly, comprising an increase of 6 and 4%, respectively. This approaches the values reported by Dauncey (7), who found an increase in 24-h EE of 7% over a comparable change in environmental temperature (6°C).

Combining the results of EE and body temperatures, we found a significant relation between the changes from *day 1* to *day 2* during the 16°C test in body temperature gradient (rectal to proximal) and the change in 24-h EE ($R^2 = 0.82$). This means that those subjects with hardly any increase in 24-h EE showed an increase or no change in the temperature gradient, whereas those with a clear increase in 24-h EE showed a decrease in the temperature gradient. In other words, there is a continuum between those subjects showing a metabolic adaptation during the two test days with a decrease of their insulative component and those showing hardly any or no metabolic adaptation, with no change or even an increase in their insulative component. The magnitude of changes within individuals (max change in EE: 1.5 MJ/day; body temperature gradient: 0.5°C) approaches the interindividual differences that may have significant physiological and clinical metabolic consequences (13, 18).

The interindividual differences in response to a cold environment implicate individual differences in energy-conserving mechanisms that may explain individual differences in predisposition to obesity. Whether these differences are of genetic origin cannot be deduced from this study. It was shown several decades ago that adaptive changes to cold exposure can be brought about experimentally in humans (6). This means that the differences in response to the mild cold can partly be explained by differences in daily living circumstances. Nevertheless, a genetic component cannot be ruled out and deserves further investigation.

We thank Paul Schoffelen for assistance with the respiration chamber measurements and Loek Wouters for helping with the body temperature registrations. We also appreciate the enthusiastic support of Heidi Strobbe and the constructive comments of an anonymous reviewer.

REFERENCES

1. Adams T and Heberling EJ. Human physiological responses to a standardized cold stress as modified by physical fitness. *J Appl Physiol* 13: 226–230, 1958.
2. Aschoff J and Wever R. Kern und Schale im Wärmehaushalt des Menschen. *Naturwiss* 45: 477–485, 1958.
3. Blaza S and Garrow JS. Thermogenic response to temperature, exercise and food stimuli in lean and obese women, studied by 24h direct calorimetry. *Br J Nutr* 49: 171–180, 1983.
4. Bouten CVC, Pannemans DLE, Westerterp KR, and Verduin M. Physical activity assessment during standardized activity in a respiration chamber: movement registration versus energy expenditure. *Int J Obes* 19: 29, 1995.
5. Bray GA, York DA, and Fisler JS. Experimental obesity—a homeostatic failure due to defective stimulation of the sympathetic nervous system. *Vitamins and Hormones*. New York: Academic, 1989.
6. Brück K, Baum E, and Schwennicke HP. Cold-adaptive modifications in man induced by repeated short-term cold-exposures and during a 10-day and -night cold-exposure. *Pflügers Arch* 321: 159–172, 1976.

7. **Dauncey MJ.** Influence of mild cold on 24 h energy expenditure, resting metabolism and diet-induced thermogenesis. *Br J Nutr* 45: 257–267, 1981.
8. **Hardy JD and Du Bois EF.** Basal metabolism, radiation, convection and vaporization at temperatures of 22 to 35°C. *J Nutr* 15: 477–497, 1938.
9. **Hardy JD and Du Bois EF.** Differences between men and women in their response to heat and cold. *Proc Natl Acad Sci USA* 26: 389–398, 1940.
10. **Iampietro PF, Goldman RF, Buskirk ER, and Bass DE.** Response of Negro and white males to cold. *J Appl Physiol* 14: 798–800, 1959.
11. **Jansky L.** Adaptability to cold: from mouse to man. In: *Thermal Physiology*. Copenhagen: Arbetslivsinstitutet, 1997, p. 163–170.
12. **Levine JA, Eberhardt NL, and Jensen MD.** Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science* 283: 212–214, 1999.
13. **Marken Lichtenbelt WD v, Westerterp-Plantenga MS, and Van Hoydonk P.** Individual variation in the relation between body temperature and energy expenditure in response to elevated ambient temperature. *Physiol Behav* 73: 235–242, 2001.
14. **Montgomery LD and Williams BA.** Effect of ambient temperature on the thermal profile of the human forearm, hand, and fingers. *Ann Biomed Eng* 4: 209–219, 1976.
15. **Ravussin E, Lillioja S, Anderson TE, Christin L, and Bogardus C.** Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest* 78: 1568–1578, 1986.
16. **Ravussin E, Lillioja S, Knowler WC, Christin L, Freymond D, Abbott WGH, Boyce V, Howard BV, and Bogardus C.** Reduced rate of energy expenditure as a risk factor of body weight gain. *N Engl J Med* 318: 467–472, 1988.
17. **Rising R, Fontvieille AM, A, Larson DE, Spraul M, Bogardus C, and Ravussin E.** Racial difference in body core temperature between Pima Indian and Caucasian men. *Int J Obes* 19: 1–5, 1995.
18. **Rising R, Keys A, Ravussin E, and Bogardus C.** Concomitant interindividual variation in body temperature and metabolic rate. *Am J Physiol Endocrinol Metab* 263: E730–E734, 1992.
19. **Schoffelen PFM, Westerterp KR, Saris WHM, and Ten Hoor F.** A dual-respiration chamber system with automated calibration. *J Appl Physiol* 83: 2064–2072, 1997.
20. **Scholander PF, Hammel HT, Hart JS, LeMessurier DH, and Steen J.** Cold adaptation in Australian aborigines. *J Appl Physiol* 13: 211–218, 1958.
21. **Schrauwen P, Marken Lichtenbelt WD v, and Westerterp KR.** Energy balance in a respiration chamber: individual adjustment of energy intake to energy expenditure. *Int J Obes* 21: 769–774, 1997.
22. **Schrauwen P, Xia J, Bogardus C, Pratley R, and Ravussin E.** Skeletal muscle UCP3 expression is a determinant of energy expenditure in Pima Indians. *Diabetes* 48: 146–149, 1998.
23. **Siri WE.** Body composition from fluid spaces and density: analysis of methods. *Techniques for Measuring Body Composition*. Washington, DC: Natl Acad Sci, 1961, p. 223–224.
24. **Webb P.** The physiology of heat regulation. *Am J Physiol Regulatory Integrative Comp Physiol* 268: R838–R850, 1995.
25. **Weir JB.** New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol* 109: 1–9, 1949.
26. **Westerterp KR, Wilson SAJ, and Rolland V.** Diet induced thermogenesis measured over 24h in a respiration chamber: effect of diet composition. *Int J Obes* 22: 1–6, 1998.
27. **Wunderlich CA.** *Temperature in Diseases: a Manual of Medical Thermometry*. London: New Sydenham Soc., 1871, vol. 49.